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Complementary and Alternative Medicine in Hospice and Palliative Care: A Systematic Review

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Complementary and Alternative Medicine in Hospice and Palliative Care: A Systematic Review

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Running Title: CAM in Hospice and Palliative Care

Abstract:

Context. The aim of palliative care is to improve quality of life for patients with serious illnesses by treating their symptoms and adverse effects. Hospice care also aims for this for patients with a life expectancy of six months or less. When conventional therapies do not provide adequate symptom management or produce their own adverse effects, patients, families and caregivers may prefer complementary or alternative approaches in their care.

Objectives. To evaluate the available evidence on the use of complementary or alternative medicine (CAM) in hospice and palliative care and to summarize their potential benefits.

Methods. A defined search strategy was used in reviewing literature from major databases. Searches were conducted using base terms and the symptom in question. Symptoms included anxiety, pain, dyspnea, cough, fatigue, insomnia, nausea, and vomiting. Studies were selected for further evaluation based on relevancy and study type. References of systematic reviews were also assessed. After evaluation using quality assessment tools, findings were summarized and the review was structured based on PRISMA guidelines.

Results. Out of 4682 studies, 17 were identified for further evaluation. Therapies included acupressure, acupuncture, aromatherapy massage, breathing, hypnotherapy, massage, meditation, music therapy, reflexology, and reiki. Many studies demonstrated a short-term benefit in symptom improvement from baseline with CAM, although a significant benefit was not found between groups.

Conclusion. CAM may provide a limited short-term benefit in patients with symptom burden. Additional studies are needed to clarify the potential value of CAM in the hospice or palliative setting.

Keywords: Complementary therapy, alternative therapy, palliative care, hospice care, symptom management, review

Introduction

About one-third of American adults have reported use of complementary and alternative medicine (CAM) including mind and body practices, among many others.^{1,2} Despite increasing use, and many CAM therapies lack sufficient, high quality evidence to support their use in the prevention and treatment of diverse conditions.³ In addition, many health care professionals continue to have inadequate knowledge about CAM therapies.

CAM therapies have been used in the palliative care and hospice settings for many years, especially in the United Kingdom. Patients in these settings commonly report a high symptom burden potentially affecting their quality of life. Distressing symptoms may be related both to the underlying disease, as well as adverse effects from treatment. As a result, when conventional therapies do not provide adequate symptom relief or produce additional adverse effects, patients, families, and caregivers may select CAM approaches, especially near the end of life.

Data from the 2007 National Home and Hospice Care Survey revealed that CAM was offered by over 40% of hospice care providers. About one-quarter of the surveyed patients received some form of a CAM therapy during hospice care. The therapies most commonly offered by hospice care providers included massage, supportive group therapy, and music therapy.⁴ The Hospice and Palliative Nurses Association (HPNA) has also recognized the prevalence and potential role of CAM in the palliative and hospice setting. The HPNA encourages the use of licensed and/or certified CAM services to provide holistic end-of-life care.⁵

With increasing support for CAM, the need for more data on different practices has continued to grow. A 2000 systematic review assessed the effectiveness of CAM therapies on selected symptoms at end of life. The authors identified that acupuncture and massage, among others, may provide pain relief while patients with end stage chronic obstructive lung disease may have less dyspnea from using acupressure and muscle relaxation.⁶ In the almost 20 years intervening, additional studies assessing the potential role of CAM therapies at the end of life have been published. The purpose of this systematic review was to identify and evaluate new evidence of

CAM therapies in managing common symptoms and improving quality of life in the palliative and hospice setting.

Methods

Protocol and Registration

The systematic review was conducted in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and is registered in the International Prospective Register of Systematic Review (PROSPERO): CRD42017067375.^{7,8}

Literature Search

A literature search was conducted in four databases including MEDLINE through PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, and Embase, for studies which assessed the efficacy of a CAM therapy in a palliative or hospice setting. The initial search was focused on the common symptoms that patients would experience in this setting.

Specific terms were used according to the database's preferred terminology. Medical subject headings (MeSH) terms, headings, thesaurus terms, and Emtree terms were used for PubMed, CINAHL, PsycINFO, and Embase, respectively. The search consisted of three base terms, "complementary medicine", "palliative care", "hospice care", and a specific symptom as a fourth term. "Complementary" was the preferred MeSH term in PubMed while "alternative" was preferred for Embase, PsycINFO, and CINAHL. Symptoms included "pain", "nausea", "vomiting", "anxiety", "cough", "fatigue", "insomnia", and "dyspnea". All are commonly reported by patients receiving palliative care, with the majority of patients diagnosed with cancer.^{6,9} Filters for study types, date range of January 1999 to May 2016, and English language were applied after entering search terms to narrow results.

A second search focused on CAM and quality of life at end of life was also conducted to include multiple symptoms and overall aspects of a patient's life. In this search, the same initial base terms,

“complementary medicine”, “palliative care”, “hospice care”, were used and the fourth term was “quality of life”. Table 1 provides an overview of the specific terms used and filters applied according to database.

A third search was conducted using the same search terms and filters for date range and English language. However, rather than filter for controlled trials, a filter for systematic reviews was applied.

Eligibility

Each author screened results from one assigned database based on title and abstract. To be eligible for review, controlled trials had to assess the efficacy of a CAM therapy in managing a symptom or quality of life in patients in a palliative or hospice setting. Systematic reviews were screened using the same eligibility criteria. Once systematic reviews were identified, their references were screened for additional controlled trials and systematic reviews that met the inclusion criteria. References of these additional sources were also screened. Meeting abstracts and quasi-experimental studies were excluded and duplicates were also removed.

Study Selection, Data Extraction, and Analysis

After compiling the full-text articles, all authors independently assessed and scored them using the Jadad scale for controlled trials. Randomization, blinding, and accountability for study participants are all factors assessed in the Jadad scale, and account for selection bias, performance and detection bias, and attrition bias, respectively.¹⁰ Studies which received a Jadad score of three or greater were included.

A meeting of the four authors was held to review Jadad scores. Disagreements were resolved by discussion of the studies and a consensus was subsequently reached. After finalizing selected articles, each author independently extracted the data which was subsequently verified by the other three authors. The study design, patient population, CAM intervention, duration of therapy, symptom(s) assessed, outcomes, measurement tools, and results were assessed.

Of the 3705 unique records identified and screened, 86 full-text articles were analyzed in depth. Of these, 69 were excluded for reasons such as inappropriate study population, resulting in 17 eligible for inclusion (Figure 1).

Results

Table 2 summarizes findings from the 17 included studies of CAM interventions in the palliative or hospice care setting. The studies which met our inclusion criteria assessed mind and body interventions. Symptoms assessed included pain, nausea and vomiting, dyspnea, anxiety and depression, and quality of life.

Many studies tested for improvement in multiple symptoms, with pain most frequently assessed (n=8). Sixteen trials enrolled patients with advanced cancer with a few including patients with other diseases and one enrolling patients with HIV/AIDS. The visual analogue scale (VAS) and Rotterdam Symptom Checklist (RSCL) were the most commonly used measurement tools. Assessment tools are described in Supplemental Table 1.

Acupressure

One study assessed the efficacy of acupressure versus sham wristbands in reducing nausea and vomiting for three days.¹¹ Measurements were recorded every 6 hours while wearing the wristbands. One patient reported mild swelling as an adverse event. Antiemetics were continued for participants, although the specific drug and administration time were not documented. The study was a pilot study and evidence of a difference between study groups was unlikely. The investigators suggested acupressure may be considered as an adjunct for palliative care patients in controlling nausea and vomiting.

Acupuncture

A pilot study evaluated the efficacy of electroacupuncture versus a palliative care nurse-led supportive care group for multiple symptoms based on the Edmonton Symptom Assessment Scale (ESAS).¹² Acupuncture points were chosen based on specific symptoms of each patient. The supportive group involved a 20 to 30-minute meeting with a palliative care nurse who provided counseling, emotional support, and coping strategies. Scores were recorded before and immediately after each intervention, and during weekly follow-ups. Acupuncture improved symptoms immediately after each session. yet ESAS scores increased by the 6-week follow-up. Right-leg stiffness and a “falling asleep” sensation were the only reported adverse effects. Nurse-led

supportive care improved symptom scores and benefit was seen at 6-week follow-up. Acupuncture may be feasible as a treatment for symptom reduction with immediate effects; however, its long-term benefits are uncertain.

Breathing

A study compared the efficacy of one versus three sessions of a complex breathing intervention.¹³ Participants reported a heavy breathlessness burden, defined by at least a score of 3 out of 10 on the Numerical Rating Scale (NRS). The group receiving three sessions had a worse baseline score in the mastery domain of the Chronic Respiratory Questionnaire – Self-Administered Survey (CRQ-SAS) while the other group had a worse baseline for anxiety. Breathing techniques included breathing training, anxiety management, relaxation, and pacing or prioritization. Secondary measures included variations of breathlessness reporting such as “average intensity”, “distress”, and “coping” using the NRS, CRQ-SAS, and HADS. A clinically significant improvement for worst breathlessness was seen; however, a “usual care” control arm was not included as a comparison for the intervention. The trial was well structured and replicable, which could warrant larger future studies.

Hypnotherapy

Two studies assessed hypnotherapy in the palliative care and hospice setting. A crossover study compared hypnotherapy to standard care on pain measures.¹⁴ In addition to hypnotherapy sessions, participants were taught self-hypnosis to use between treatment sessions. Symptoms were rated using the MYMOP Version 2 (MYMOP2) tool at baseline, week 4, and week 8. In addition to pain, effects on anxiety, insomnia, depression, headache, and desire to stop smoking were assessed. No study personnel confirmed the usage of proper technique or adherence to the assigned self-hypnosis, allowing for questions of the quality of the intervention. Because patients chose their most burdensome symptoms, multiple symptoms were evaluated; therefore, identifying the specific symptom(s) that hypnotherapy affects may be difficult.

A second study compared the effects of hypnotherapy to standard care on quality of life, anxiety, and depression.¹⁵ Patients rated their symptoms on their first visit and upon completion of the intervention. Missing RSCL subscale values were substituted using the personal scale mean of the respective respondent if at least 50% of the items on the subscale were completed. Substituting incomplete data would affect the results and the true efficacy of the intervention would be unclear. Symptom management was conducted with medications and was not evaluated in depth. Therefore, the effect of hypnosis versus medications on symptoms remains unclear. Benefit was noted in the hypnosis group and supportive group which suggests that some form of cognitive intervention may assist patients at end of life with coping.

Massage Therapy Alone

Seven studies have evaluated the efficacy of massage therapy; three were of massage therapy alone, three of massage combined with aromatherapy, and one assessed massage in combination with meditation.

One study recruited 509 patients with 380 randomized to six 30-minute individualized massage sessions by a licensed massage therapist or simple touch.¹⁶ A similar proportion of patients in both groups previously received massage therapy; baseline pain scores were also similar between groups. Secondary measurements include the MPAC mood scale and the McGill Quality of Life Questionnaire. Scores were recorded at baseline, weeks 1 and 2, and 1.5 weeks after the intervention completion. Two serious adverse events were reported in the massage group (respiratory infection and gastrointestinal bleed), but were deemed unrelated to treatments. No control group was included which would have assisted in differentiating a true benefit from massage therapy. The study is notable because of its large, multisite design and shows some statistically significant immediate benefits with massage therapy. The short study period may have accounted for failure to detect a significant difference in sustained, longer term scores.

A Spanish trial evaluated the effects of physical therapy, including massage and exercise, in patients with advanced cancer.¹⁷ Of 92 patients screened for eligibility, 24 were enrolled; three quarters were men and half had lung cancer. The intervention group received six physiotherapy sessions which consisted of several

massage techniques, mobilization, and local and global exercises performed by a therapist. Pre- and post-intervention scores assessed changes in pain while the mood portion of the MPAC and the Memorial Symptom Assessment Scale (MSAS) evaluated mood. Only 15 patients were assessed in the final analysis. Multiple techniques were implemented in the massage group and no standardized protocol was available for the trial to be replicated. Techniques were chosen according to the type of cancer, which may warrant further study into specific massage techniques to provide optimal symptom control.

Another study compared a standardized massage or usual hospice care.¹⁸ During enrollment, none of the participants reported receiving massage therapy. All staff were blinded to subject group assignment except for the person who received eligibility forms and a social worker who scheduled the massage therapists. Although a standardized protocol for massage was created, sessions were still individualized and the duration varied from 30 to 50 minutes. After the intervention, a few subjects reported receiving previous massage therapies prior to enrollment. Several subjects received additional massage sessions in between the study sessions. While the study did not report a significant difference with individuals receiving additional massages, the quality of the study intervention is questionable. The results may have been affected as a result of receiving more sessions and from an unknown source.

Massage and Aromatherapy

A single-blinded study evaluated the long-term benefits of aromatherapy massage with lavender oil versus massage with an inert oil versus no massage.¹⁹ Enrollment fell short of the 15 patients needed in each study arm to detect a 2.3-point difference on the VAS. Six patients withdrew as a result of death or feeling unwell. Groups were similar at baseline except the massage only group had a significantly higher RSCL score. Analyses were performed for the three study groups and an additional combined aromatherapy and massage group. The combined aromatherapy and massage group was not included as an initial study group to which participants were randomized. While not mentioned in the methodology section, results from the combined group were presented in the analysis; this is an important consideration when evaluating the analyses.

Another pilot study tested the feasibility of aromatherapy massage in patients with cancer. Of 46 patients recruited from a palliative day care center, 29 completed the trial.²⁰ The aromatherapy massage and control groups had similar mean performance status scores of 1.4 and 1.3, respectively. Six patients in the control group were taking antidepressants compared to none in the aromatherapy massage group. Adverse effects were limited to a rash following massage. A high withdrawal rate impacts assessment of the intervention and larger studies are needed.

Aromatherapy massage versus massage with an inert oil were compared for their effect on anxiety and quality of life.²¹ At baseline, patients randomized to aromatherapy reported poorer quality of life compared with those in the massage group. Quality of life (QoL) was measured at baseline and one week after the last massage was administered. Anxiety scales were administered before and after each massage. Significantly greater improvement in RSCL subscales was noted for the aromatherapy group, despite a poorer baseline QoL. Further study into the specific essential oil used may be warranted to determine the impact on symptom improvement. No entry criteria were required for the study and a control group was not used. The lack of a control group is important as each modality has yet to be proven beneficial as individual treatments.

Massage and Meditation

A study evaluated both meditation and massage for improving QoL near end of life.²² A total of 106 patients were screened with 58 randomized to one of four groups. Despite randomization, baseline characteristics in the study groups varied. The standard care group had higher mean viral load while the combined meditation and massage group had the highest CD4 count. Differences in baseline characteristics could affect the results of the interventions depending on patient health status. Responses were recorded at baseline, at the end of weeks 2 and 4 during the intervention period, and 1-month after the intervention (week 8). The combined meditation and massage group demonstrated the greatest overall improvement even after multivariate adjustment for baseline differences. However, because the combined group had a higher CD4 count

and a lower viral load at baseline, the results may reflect better participant disease control in comparison to the other groups.

Music Therapy

A palliative care team analyzed 198 patients with advanced, life-limiting illness.²³ The music therapy group received 20-minute music therapy sessions performed by a music therapist. Each music therapy session was individualized, although a standardized framework for the sessions was implemented. The control group received the same comfort measures as the music therapy group during the session; however, a music therapist was not present. Both groups had similar baseline characteristics. Pain was assessed at pre- and post-intervention. Although 20 minutes was allotted, a few accounts of up to 50 minutes were noted. As a result, the timing of the post-intervention score also varied. Blinding was broken for a few patients because participants revealed their group assignment to the research assistant. Only immediate effects were studied, so the long-term benefits are unknown.

In an Australian study, 25 patients were recruited from inpatient hospice services.²⁴ Only age, sex, and diagnosis were reported for baseline characteristics. Music session length varied from 20-40 minutes and any sessions outside of the study's session duration were not included in the data. Therefore, data could be missing that would affect the overall results. Only pre- and post-intervention scores were recorded so only short-term effects were assessed. Patients in the control group continued to receive music therapy outside of the study, making it unclear if the control group was a true control with no pre-exposure to music therapy. Both studies showed music therapy improved symptom burden; participants requested and continued receiving music therapy outside of the studies.

Reflexology

Two studies assessed the efficacy of reflexology in improving QoL. One study randomized 12 patients receiving palliative care to receive reflexology or placebo.²⁵ Interventions were carried out on days 1, 3, and 5; assessments using the VAS were recorded at baseline and after the intervention. Multiple symptoms were

assessed including appetite, breathing, communication, constipation, pain, and tiredness. Although the reflexologist could avoid reflexology points to simulate “placebo reflexology”, some skill may still remain in providing patients relief through a foot massage. Overall, patients reported an improvement in QoL, but with the short duration and small population, the generalizability of the study to other care centers is difficult.

In the second trial, patients who were not receiving active cancer treatment were recruited to receive reflexology or foot massage.²⁶ Seventeen patients were included in the analysis. Participants and interviewers were blinded to the intervention. “Placebo” foot massage may have provided some level of relief for the patients. Neither group demonstrated significant improvement in mood and the study failed to demonstrate superiority of reflexology over foot massage. Foot discomfort was the predominant adverse effect, along with nausea, shaking, and sleep disturbances. Both studies used foot massage as a placebo”, but the benefit of massage alone may have occurred.

Reiki

One trial assessed reiki for improvement in pain and QoL.²⁷ Of 73 patients screened for eligibility, 24 were enrolled. Participants received varying amounts of opioids, but were all considered to be opioid tolerant as defined by having a dose increase of over 5% per day. Eleven patients were taking less than 60 mg of morphine per day, eight received between 60-300 mg/day and five were taking over 300 mg/day. Primary outcome measures were assessed on days 1 and 4. Quality of life was assessed using ESAS. The use of objective outcome measures could provide more evidence if a placebo effect was present. Although no difference was found between the two groups, the study was practical because it also assessed conventional treatment. Reiki as an adjunct to opioid therapy warrants further study with a larger cohort and longer study period.

Discussion

This systematic review of randomized controlled trials was conducted to evaluate the newer evidence available since the 2000 publication by Pan and colleagues.⁶ The older databases, CancerLIT and AIDS-LINE,

have since been incorporated into MEDLINE, resulting in fewer and more comprehensive databases from which our searches were conducted. No randomized controlled trials of herbal products or dietary supplements were identified in the literature search, resulting in the included studies evaluating mind and body CAM. Using the Jadad scale, we identified higher quality studies on CAM in the palliative or hospice setting.

Massage therapy, combined with aromatherapy, meditation, or massage alone, were the most common CAM assessed in our systematic review. Studies that assessed massage therapy alone and massage combined with meditation demonstrated improvement in pain and QoL when compared to control. Mixed results were found in studies with massage with aromatherapy. Two studies reported no significant change in QoL or pain while the third aromatherapy massage study reported improvement in anxiety. A decrease in anxiety and pain was observed in patients who received music therapy, although blinding to intervention and additional therapy sessions were concerns. No difference in QoL or symptom improvement was seen in hypnotherapy trials. Of the other CAM, reiki produced a significant decrease in pain intensity although one study was underpowered.

This systematic review has several limitations. While we had defined CAM by the National Center for Complementary and Integrative Health's definition, variations of the word exist. By exploding each database's index terms, the number of terms under "Complementary therapies" or "Alternative therapies", varied greatly as well as what was considered "CAM" (Supplemental Figure 1). Potential studies that did not list our index terms may have not populated in the search results. Our search strategy did not include the term integrative medicine which has been increasing in use to describe CAM. Excluding this term may have resulted in additional missed studies.

Our search terms included "palliative care" or "hospice care". While those enrolled in hospice care receive palliative care, not all patients receiving palliative care may be near end of life. A few studies included patients enrolled in palliative care only and no specifications were stated on whether patients were still receiving active treatment. Therefore, the characteristics of the patient population may vary and affect how patients may feel or perform overall.

The Jadad scale was used as the evaluation tool to decide which studies to include in the review. Despite the tool's simplicity, our authors' scores were inconsistent at times and differences were resolved through discussions involving all authors. The reasons for variability in Jadad scores included ambiguity of the studies and differing opinions. While all studies included scored a three or higher on the Jadad scale, many other characteristics differed between the articles. For example, one study enrolled a total of eight patients while another study enrolled 200 patients.^{11,23}

Various study designs were used and what was considered "control" or "placebo" differed among the studies. Depending on what one considers as "CAM", the control group of a study may be considered another CAM. One such example is the reflexology study conducted by Hodgson et al in which the "placebo reflexology" was a gentle foot massage.²⁶ In addition, by the nature of mind and body CAM, true blinding of the participants and performers is difficult. Some methods have been developed to provide blinding of CAM such as sham acupuncture. However, sham acupuncture has mixed results on its reliability as a placebo.²⁸ We were unable to perform a meta-analysis as a result of the varying measurement tools used by the studies we evaluated. Additionally, the majority of measurement tools were subjective. A few studies used objective measurements, such as blood pressure or respiratory rate.²⁰ Not all studies performed statistical analyses and one study that did reported failure to account for multiple testing.²⁰ In addition, multiple studies assessed quality of life which encompasses multiple symptoms. As a result, determining what symptoms benefit most from a CAM intervention is difficult since multiple symptoms were evaluated simultaneously.

Enrollment rates for studies were low despite recruitment periods of a few years in several studies.¹² In addition, as a typical finding in the hospice care setting, many participants withdrew because of poor health or death. The high withdrawal rate further decreases the small population size and many studies were unable to provide power calculations to conclude any significance. Taking this into account, some studies had broader inclusion criteria to recruit as many participants as possible. However, in doing so, a diverse population in which treatments and demographic characteristics vary greatly among patients resulted. A few studies addressed

concomitant use of drug therapy, but did not specify the drugs used or duration of drug therapy.^{11,13} Studies were conducted in multiple countries, such as the United Kingdom or Spain.^{18,21} The applicability of such studies should be taken into account as the patient population and treatment modalities may differ depending on the country. Baseline scores for patients' reported symptoms also differed between study groups in several studies, which could affect the results of how well the intervention managed the symptom(s) in question.

Although limitations are apparent, our review identified new studies which show a modest benefit in improvement of patients' quality of life and symptoms. Despite few studies reporting statistically significant changes in symptom improvement, clinically significant changes were documented and patients reported positive outcomes in interviews and on questionnaires. Adverse effects were uncommon and minor in nature. A professional in the specific CAM approach was recruited to perform the intervention in multiple studies. The expertise of the CAM provider is important to ensure the highest quality of CAM is given.

We identified common outcome measures which may be considered for future studies. A possible meta-analysis may be performed if new studies used the same measures. Our work has also identified barriers to CAM studies which may be taken into consideration, such the lack of a universal assessment tool or accepted placebo for proper assessment of a CAM. Small patient populations and short study periods are additional barriers to providing a higher quality study to demonstrate adequate power. A few studies simultaneously assessed multiple CAM modalities, making it difficult to identify which therapy provides more benefit. For patients who are interested in CAM, a discussion should be held with their healthcare providers about potential value and considerations.

Conclusions

Since 2000, additional studies evaluating CAM in the palliative and hospice setting have been published. This systematic review identified and evaluated pilot studies testing the feasibility of a CAM intervention in the palliative or hospice setting as well as larger trials of a previously tested CAM. Of the studies reviewed, a modest short-term benefit was observed in some trials. Future studies should consider a multicenter design to

recruit more patients. One CAM modality should be assessed at a time and a universal tool for evaluating symptom improvement should be established for consistency. Of the CAM interventions summarized, music therapy, massage therapy, and reiki had the most potential benefit although all studies had significant limitations. Continued research is essential to provide the best patient care in hospice and palliative care.

Disclosures

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28. Lundeberg T, Lund I, Näslund J, Thomas M. The Emperors sham: wrong assumption that sham needling is sham. *Acupunct Med* 2008;26:239–42.

Figures and Tables:

Figures:

- Figure 1: Flow Diagram of Steps in Systematic Review
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Table 1
Summary of Search Strategies and Number of Results

Database	Search Terms	Symptoms + “Quality of life”	Applied Filters	No. Results ^a
MEDLINE (PubMed)	((("Complementary Therapies"[Mesh]) AND ("Hospice and Palliative Care Nursing"[Mesh] OR "Palliative Care"[Mesh] OR "Palliative Medicine"[Mesh] OR "Hospice Care"[Mesh])) AND "SYMPTOM"[Mesh])	"Pain"[Mesh] "Dyspnea"[Mesh] "Cough"[Mesh] "Nausea"[Mesh] "Vomiting"[Mesh] "Anxiety"[Mesh] "Sleep Initiation and Maintenance Disorders"[Mesh] "Fatigue"[Mesh]	<u>Study Types:</u> Clinical study/trial Controlled clinical trial Randomized controlled trial Systematic reviews Meta-analysis Multicenter study Observational study <u>Date:</u> 1999-2016	140
CINAHL	(MH "Alternative Therapies+") AND ((MH "Palliative Care") OR (MH "Hospice and Palliative Nursing") OR (MH "Terminal Care") OR (MH "Hospice Care")) AND (MH “SYMPTOM”)	(MH “Pain+”) (MH “Dyspnea”) (MH “Nausea+”) (MH “Nausea and Vomiting”) (MH “Vomiting”) (MH “Anxiety+”) (MH “Insomnia+”) (MH “Fatigue+”)	<u>Study Types:</u> Clinical trial Meta-analysis Randomized controlled trial Research Systematic review <u>Date:</u> January 1999-May 2016	197
Embase	'alternative medicine'/exp AND 'palliative therapy'/exp OR 'palliative nursing'/exp AND SYMPTOM/exp	'pain'/exp 'dyspnea'/exp 'coughing'/exp NOT 'pertussis' NOT 'experimental coughing' 'nausea'/exp 'vomiting'/exp NOT 'experimental emesis' 'anticipatory nausea and vomiting'/exp 'chemotherapy induced emesis'/exp 'chemotherapy induced nausea and vomiting'/exp	<u>Study Types:</u> Clinical trial Prospective study Randomized controlled trial	458

		'radiation induced emesis'/exp 'nausea and vomiting'/mj 'anxiety'/exp 'insomnia'/exp 'fatigue'/exp NOT 'persian gulf syndrome' NOT 'postviral fatigue syndrome'	Systematic review Retrospective study <u>Date:</u> 1999-2016	
PsycINFO	SU.EXACT.EXPLODE("Alternative Medicine") AND SU.EXACT.EXPLODE("Palliative Care") OR SU.EXACT.EXPLODE("Hospice") AND SU.EXACT.EXPLODE("SYMPTOM")	SU.EXACT.EXPLODE("Pain") SU.EXACT.EXPLODE("Dyspnea") SU.EXACT.EXPLODE("Nausea") SU.EXACT.EXPLODE("Vomiting") SU.EXACT.EXPLODE("Anxiety") SU.EXACT.EXPLODE("Insomnia") SU.EXACT.EXPLODE("Fatigue")	<u>Methodology:</u> Follow-up study Meta-analysis Prospective study Systematic review Treatment outcome/clinical trial <u>Date:</u> After December 31, 1998- May 2016	695

Table 1. Summary of Search Strategies and Number of Results. This chart demonstrates the search strategy used, including search terms and filters used for each database and the number of results produced. Included terms are specific to their respective database. A separate search was conducted for each symptom listed. Not all databases included a symptom of interest (i.e. "Cough" was not a valid search term in CINAHL)

^a=With duplicates removed

Table 2
Summary of Articles Included in Systematic Review

Primary Author (Year)	Study Design	Patient Population ^a	Interventions	Duration of Study	Primary Symptom(s) Assessed	Primary Outcome	Results
<i>Acupressure</i>							
Perkins, P (2008)	R, SB, C	<ul style="list-style-type: none"> 8 patients with terminal cancer Median age 61 years (range 48-74 years) 	<ul style="list-style-type: none"> Acupressure wristbands (P6 pressure point) (n=3) Sham wristbands (n=5) 	3 days	<ul style="list-style-type: none"> Nausea Vomiting 	<ul style="list-style-type: none"> VAS Total antiemetic doses Antiemetic escalation Change in emesis episodes from baseline 	<ul style="list-style-type: none"> No evidence of difference between two groups for any endpoint SSC: 23, 15, and 15 patients needed in each group to show difference between change from baseline emesis, antiemetic doses, and VAS score
<i>Acupuncture</i>							
Lim, JTW (2011)	R, NB, C	<ul style="list-style-type: none"> 18 patients with incurable cancer EG: mean age 55 ± 11.1 years (range 31-72; 8 women, 2 men) CG: mean age 64.9 ± 8.7 years (range 53-81; 7 women, 1 man) 	<ul style="list-style-type: none"> Acupuncture (n=10) Nurse-led supportive care (n=8) 	4 weeks (weekly follow-up for 6 weeks after final intervention)	<ul style="list-style-type: none"> Pain Tiredness Nausea Depression Anxiety Drowsiness Loss of appetite Lack of wellbeing SOB 	<ul style="list-style-type: none"> ESAS 	<ul style="list-style-type: none"> Total ESAS scores were reduced by 19% for EG (mean change -0.77 [range -2.75 to 1.5]) and 26% for CG (mean change -1.69 [range -2.25 to -0.25]) comparing baseline to week 6 after final intervention Only descriptive statistics were used because of small sample size.
Soden, K (2004)	R, SB, C	<ul style="list-style-type: none"> 42 patients with advanced cancer Median age 73 years (range 44-85) 32 women, 10 men 	<ul style="list-style-type: none"> Aromatherapy massage with lavender oil (n=16) Massage with inert oil only (n=13) No massage (n=13) 	4 weeks	<ul style="list-style-type: none"> Pain 	<ul style="list-style-type: none"> VAS (primary endpoint) Modified Tursky Pain Descriptors Scale VSH HADS RSCL 	<ul style="list-style-type: none"> No statistically significant changes in pain from baseline to end of study for any group After second treatment, a reduction in pain VAS scores in both aromatherapy (P = 0.03) and combined massage (P = 0.01) was observed
Wilcock, A (2004)	R, NB, C	<ul style="list-style-type: none"> 29 patients with cancer EG: mean age 70 years CG: mean age 73 years 	<ul style="list-style-type: none"> Aromatherapy massage with day care (n=11) Day care only (n=18) 	4 weeks	<ul style="list-style-type: none"> QoL Physical symptoms Mood 	<ul style="list-style-type: none"> MYMOP – Quality of Life POMS – Mood 	<ul style="list-style-type: none"> No statistically significant differences in outcomes between groups Mean difference in slope for POMS total score -0.4 (95% CI -3.4, 2.5) Mean difference in slope for QoL -0.2 (95% CI -0.6, 0.2)

Wilkinson, S (1999)	R, NB, C	<ul style="list-style-type: none"> 87 patients with cancer Mean age 53.5 years 78 women, 9 men 	<ul style="list-style-type: none"> Aromatherapy massage with Roman chamomile oil (n=43) Massage with inert oil only (n=44) 	4 weeks	<ul style="list-style-type: none"> QoL Anxiety 	<ul style="list-style-type: none"> RSCL STAI 	<ul style="list-style-type: none"> Pre- and post-test scores for severe physical symptoms ($P < 0.05$), psychological ($P < 0.001$), and QoL ($P < 0.01$) with EG showed improvement Pre- and post-test scores for anxiety were reduced in both groups ($P < 0.0001$)
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Breathing

Johnson, MJ (2015)	R, NB, C	<ul style="list-style-type: none"> 124 patients with intrathoracic malignancy and breathlessness^b One session: mean age 70 ± 9 years Three sessions: mean age 69 ± 11 years 	<ul style="list-style-type: none"> One breathing session (n=43) Three breathing sessions (n=81) 	4 weeks (with a follow-up at 8 weeks)	<ul style="list-style-type: none"> Breathlessness 	<ul style="list-style-type: none"> NRS (Worst breathlessness score) 	<ul style="list-style-type: none"> Overall decrease in “worst score” from 6.81 ± 1.89 at baseline to 5.84 ± 2.39 at week 4 No between arm differences in “worst breathlessness” NRS score between study groups; mean difference 0.2 (95% CI -2.31, 2.97) SSC: 146 participants needed to determine difference in AUC for improvement of breathlessness
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Hypnotherapy

Harlow, T (2015)	R, NB, CS	<ul style="list-style-type: none"> 11 patients with a primary diagnosis of cancer^b Mean age 57 years 	<ul style="list-style-type: none"> Hypnotherapy Group A (n=9, 4 weeks of hypnotherapy then 4 weeks off) Group B (n=2, 4 weeks off then 4 weeks hypnotherapy) 	8 weeks	<ul style="list-style-type: none"> Pain 	<ul style="list-style-type: none"> MYMOP (version 2) 	<ul style="list-style-type: none"> No significant reduction in pain for patients who identified pain as primary symptom SSC: 168 patients needed to detect a meaningful symptom change
Lioffi, C (2001)	R, SB, C	<ul style="list-style-type: none"> 50 patients with advanced cancer Age range 35-74 years 	<ul style="list-style-type: none"> Hypnotherapy with standard care (n=25) Standard care only (n=25) 	4 weeks	<ul style="list-style-type: none"> QoL Depression Anxiety 	<ul style="list-style-type: none"> RSCL HADS 	<ul style="list-style-type: none"> For both groups, post-intervention scores improved for all measured outcomes compared with baseline HADS anxiety and depression scores decreased in the EG compared with CG ($P < 0.01$) RSCL subscales for psychological distress, physical distress, and activity level were improved for EG vs CG ($P < 0.01$)

Massage Therapy Only

Kutner, JS (2008)	R, SB, C	<ul style="list-style-type: none"> 380 patients with solid tumors and metastases 	<ul style="list-style-type: none"> Massage therapy (n=188) Simple touch (n=192) 	3 weeks	<ul style="list-style-type: none"> Pain 	<ul style="list-style-type: none"> MPAC (Immediate pain) BPI (Sustained pain) 	<ul style="list-style-type: none"> MPAC scores showed clinically significant improved in massage group (-1.87 points [95% CI, -2.07, -1.67])
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		<ul style="list-style-type: none"> EG: mean age 65.2 ± 14.4 years CG: mean age 64.2 ± 14.4 years 					<ul style="list-style-type: none"> EG superior to touch directly after treatment, but not clinically significant (mean pain difference - 0.90 points [95% CI, -1.19, -0.61]) For BPI, no statistically or clinically significant difference between arms SSC: 440, assuming 30% attrition, to detect clinically meaningful differences between study groups
Lopez-Sendin, N (2012)	R, SB, C	<ul style="list-style-type: none"> 24 patients with terminal cancer EG: mean age 55 ± 21 years CG: mean age 54 ± 8 years 	<ul style="list-style-type: none"> Physiotherapy (n=12) Simple touch (n=12) 	2 weeks	<ul style="list-style-type: none"> Pain Mood 	<ul style="list-style-type: none"> MPAC (Pain and mood) BPI (Sustained pain) 	<ul style="list-style-type: none"> No significant group x time interaction for MPAC mood differences <i>Post-hoc</i> analysis demonstrated potential improvements in worst and current pain SSC: 12 subjects per group needed to detect difference in BPI score
Wilkie, DJ (2000)	R, SB, C	<ul style="list-style-type: none"> 29 patients with cancer^b Mean age 63 years (range 30-87) 20 men, 9 women 	<ul style="list-style-type: none"> Massage with hospice care (n=26) Hospice care only (n=30) 	3 weeks	<ul style="list-style-type: none"> Pain QoL 	<ul style="list-style-type: none"> Pain Assessment Tool Skilled Nursing Visiting Report Form HR RR Graham QoL Tool 	<ul style="list-style-type: none"> Some significant reductions in HR and RR after massage sessions Reduced pain intensity immediately after 1st and 3rd massages (P<0.09) Reduction in pain was not significant between study groups. No significant differences between groups for QoL scores

Massage and Aromatherapy

Soden, K (2004)	R, SB, C	<ul style="list-style-type: none"> 42 patients with advanced cancer Median age 73 years (range 44-85) 32 women, 10 men 	<ul style="list-style-type: none"> Aromatherapy massage with lavender oil (n=16) Massage with inert oil only (n=13) No massage (n=13) 	4 weeks	<ul style="list-style-type: none"> Pain 	<ul style="list-style-type: none"> VAS (primary endpoint) Modified Tursky Pain Descriptors Scale VSH HADS RSCL 	<ul style="list-style-type: none"> No statistically significant changes in pain from baseline to end of study for any group After second treatment, a reduction in pain VAS scores in both aromatherapy (P = 0.03) and combined massage (P = 0.01) was observed
Wilcock, A (2004)	R, NB, C	<ul style="list-style-type: none"> 29 patients with cancer EG: mean age 70 years CG: mean age 73 years 	<ul style="list-style-type: none"> Aromatherapy massage with day care (n=11) Day care only (n=18) 	4 weeks	<ul style="list-style-type: none"> QoL Physical symptoms Mood 	<ul style="list-style-type: none"> MYMOP – Quality of Life POMS – Mood 	<ul style="list-style-type: none"> No statistically significant differences in outcomes between groups Mean difference in slope for POMS total score -0.4 (95% CI -3.4, 2.5) Mean difference in slope for QoL -0.2 (95% CI -0.6, 0.2)
Wilkinson, S (1999)	R, NB, C	<ul style="list-style-type: none"> 87 patients with cancer 	<ul style="list-style-type: none"> Aromatherapy massage with 	4 weeks	<ul style="list-style-type: none"> QoL Anxiety 	<ul style="list-style-type: none"> RSCL STAI 	<ul style="list-style-type: none"> Pre- and post-test scores for severe physical symptoms (P < 0.05), psychological (P < 0.001), and QoL

		<ul style="list-style-type: none"> • Mean age 53.5 years • 78 women, 9 men 	<ul style="list-style-type: none"> • Roman chamomile oil (n=43) • Massage with inert oil only (n=44) 				<ul style="list-style-type: none"> • (P < 0.01) with EG showed improvement • Pre- and post-test scores for anxiety were reduced in both groups (P < 0.0001)
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Massage and Meditation

Williams, A (2005)	R, SB, C	<ul style="list-style-type: none"> • 58 patients with HIV/AIDS • Meditation: mean age 45.08 ± 2.2 years • Massage: mean age 42.81 ± 2.2 years • Meditation and massage: mean age 47.31 ± 2.25 years • Control: mean age 45.56 ± 2.24 years • 43% women 	<ul style="list-style-type: none"> • Meditation only (n=13) • Massage therapy only (n=16) • Meditation and massage therapy (n=13) • Control (standard care) (n=16) 	8 weeks	• QoL	• MVQOLI	<ul style="list-style-type: none"> • Combined group improvement for total score (3.75 ± 1.1 [P<0.05] and transcendent (5.92 ± 2.06 [P<0.05]) compared to other groups at 8 weeks • Function score improved in combined group (19.08 ± 5.48 [P<0.05]) compared to massage and CG at 8 weeks • QoL improvements remained after multivariate adjustment for group differences at baseline • SSC: 40 subjects to detect a 5 point difference on MVQOLI between the combined and standard care groups
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Music Therapy

Gutgsell, KJ (2013)	R, SB, C	<ul style="list-style-type: none"> • 200 patients with terminal illness • EG: mean age 57.45 ± 14.76 years • CG: mean age 54.72 ± 15.34 years • 69% women 	<ul style="list-style-type: none"> • Music therapy and comfort measures (n=100) • Comfort measures only (n=100) 	20-50 minutes (One music therapy session)	• Pain	• NRS	<ul style="list-style-type: none"> • Decline (improvement) from pre- to post-test NRS for EG (mean change -1.94 [95% CI -2.37, -1.52]) and CG (mean change -0.56 [95% CI -0.92, -0.19]) • Greater decline in NRS score in the EG (difference in means -1.39 [95% CI -1.95, -0.83]) • SSC: 100 subjects per treatment arm to show differences in mean post-test NRS
Horne-Thompson, A (2008)	R, SB, C	<ul style="list-style-type: none"> • 25 patients (24 with cancer) • EG: mean age 76.2 ± 10.36 years • CG: mean age 71.4 ± 16.05 years 	<ul style="list-style-type: none"> • Music therapy (n=13) • Volunteer led therapy session without music (n=12) 	20-40 minutes (One music therapy session)	• Anxiety	<ul style="list-style-type: none"> • ESAS • HR 	<ul style="list-style-type: none"> • Anxiety using ESAS was reduced for EG (P=0.005), although post-intervention data not reported • No difference between study groups for anxiety as demonstrated by decrease in HR (P=0.8) • SSC: 60 subjects to demonstrate a difference between groups

Reflexology

Hodgson, H (2000)	R, SB, C	<ul style="list-style-type: none"> 12 patients with cancer Age range 58-80 years 	<ul style="list-style-type: none"> Reflexology (n=6) Gentle foot massage ("placebo" reflexology) (n=6) 	5 days	<ul style="list-style-type: none"> QoL 	<ul style="list-style-type: none"> VAS 	<ul style="list-style-type: none"> Breathing subscale of VAS improved with reflexology (mean change 2.2; $P<0.05$ between groups) Overall improvement in QoL scores improved for EG ($P=0.004$ between groups; data not provided)
Ross, CSK (2002)	R, DB, C	<ul style="list-style-type: none"> 17 patients with advanced cancer^b Mean age 74 years (range 57-85) 7 men, 10 women 	<ul style="list-style-type: none"> Reflexology (n=7) Simple foot massage (n=10) 	6 weeks	<ul style="list-style-type: none"> Mood 	<ul style="list-style-type: none"> HADS Symptom Distress Score 	<ul style="list-style-type: none"> HADS scores remained stable for both study groups from baseline to six weeks No significant difference between groups except for improvement in appetite and mobility in foot massage group
<i>Reiki</i>							
Olson, K (2003)	R, NB, C	<ul style="list-style-type: none"> 24 patients with advanced cancer^b 79% solid tumors 9 men; mean age 59.5 years 15 women; mean age 56 years 	<ul style="list-style-type: none"> Reiki (n=11) Rest (n=13) 	7 days	<ul style="list-style-type: none"> Pain 	<ul style="list-style-type: none"> VAS SBP/DBP HR RR 	<ul style="list-style-type: none"> Improvement with EG reported for pain ($P=0.035$), drop in DBP ($P=0.005$) and HR ($P=0.005$) compared to rest on day one No significant difference in pain or median morphine equivalent dose from day one to day seven between study groups SSC: 100 subjects to detect a 20% reduction in VAS pain score

Table 2. Summary of Articles Included in Systematic Review. This chart outlines characteristics of studies included in the systematic review.

AUC=Area Under Curve. BPI=Brief Pain Inventory. C=Controlled. CG=Control Group. CS=Crossover Study. DB=Double Blinding. DBP=Diastolic Blood Pressure. EG=Experimental Group. ESAS=Edmonton Symptom Assessment Scale. HADS=Hospital Anxiety and Depression Scale. HIV/AIDS=Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome. HR=Heart Rate. MPAC=Memorial Pain Assessment Card. MSE=Mean Squared Errors. MVQOLI=Missoula-VITAS Quality of Life Index. MYMOP=Measure Your Medical Outcomes Profile Scores. NB=No Blinding. NRS=Numerical Rating Scale. POMS=Profile of Mood State. QoL=Quality of Life. R=Randomized. RR=Respiratory Rate. RSCL=Rotterdam Symptom Checklist. SBP=Systolic Blood Pressure. SOB=Shortness of Breath. SSC=Sample Size Calculation. SB=Single Blind. STAI=State Trait Anxiety Inventory. VAS=Visual Analog Scale. VSH=Verran and Snyder-Halpern sleep scale

^a=Baseline characteristics are listed as reported in study (i.e. Some studies analyzed characteristics of the whole study population while other studies analyzed characteristics of individual study groups)

^b=Number represents evaluable participants and does not include excluded participants originally randomized

Supplemental Table 1
Description of Validated Assessment Tools used in Studies

Tool	Use	Subscales	Scores
ESAS ¹	Assess nine common symptoms experienced by patients receiving palliative care using VAS	<ul style="list-style-type: none"> • Pain • Activity • Nausea • Depression • Anxiety • Drowsiness • Appetite • Wellbeing • Shortness of Breath 	<ul style="list-style-type: none"> • 0–100mm • 0 – Symptom is absent • 100 – Worst possible severity <p>Higher numbers indicate worse outcomes</p>
Graham's QoL Tool ²	Measure perceived QoL in patients with melanoma	<ul style="list-style-type: none"> • GWBS • CQLS • SCQLS 	<p>GWBS:</p> <ul style="list-style-type: none"> • 1–10 • 1 – “poorer than most” • 10 – “very much better than most” <p>CQLS</p> <ul style="list-style-type: none"> • 1–10 • 1 – Poor • 10 – Excellent <p>SCQLS:</p> <ul style="list-style-type: none"> • 1–10 • 1 – Not at all satisfied • 10 – Very satisfied <p>Lower numbers indicate worse outcomes</p>
HADS ³	Detect states of depression and anxiety in the setting of a hospital medical outpatient clinic	<ul style="list-style-type: none"> • Anxiety • Depression 	<p>Anxiety/Depression Subscales</p> <ul style="list-style-type: none"> • 1–3 • 1 – Not at all • 3 – Very often <p>Overall:</p> <ul style="list-style-type: none"> • 0–7 = Normal • 8–10 = Mild • 11–14 = Moderate • 15–21 = Severe <p>Higher numbers indicate worse outcomes</p>
McGill QoL Questionnaire ⁴	Assess QoL in patients with a life-threatening disease in a palliative care setting	<ul style="list-style-type: none"> • Physical symptoms • Psychological symptoms • Existential wellbeing • Support 	<ul style="list-style-type: none"> • 0–10 • 0 – Least desirable situation • 10 – Most desirable situation <p>Lower numbers indicate worse outcomes</p>
MYMOP/MYMOP2 ⁵	Evaluate patient-generated measures over time	<ul style="list-style-type: none"> • Symptom 1 • Symptom 2 • Activity 	<ul style="list-style-type: none"> • 0–6 • 0 – As good as it could be • 6 – As bad as it could be <p>Higher numbers indicate worse outcomes</p>

MPAC ⁶	Assess pain and distress in patients with cancer	<ul style="list-style-type: none"> • Mood Scale • Pain Scale • Pain Description Scale • Relief Scale 	<p>Mood Scale</p> <ul style="list-style-type: none"> • Worst mood to Best mood <p>Lower scores indicate worse outcomes</p> <p>Pain Scale</p> <ul style="list-style-type: none"> • Least possible pain to Worst possible pain <p>Higher numbers indicate worse outcomes</p> <p>Pain Description Scale</p> <ul style="list-style-type: none"> • No pain • Weak • Mild • Just noticeable • Moderate • Strong • Severe • Excruciating <p>Relief Scale</p> <ul style="list-style-type: none"> • No relief of pain to Complete relief of pain <p>Lower scores indicate worse outcomes</p>
MSAS ⁷	Evaluate symptom prevalence, characteristics, and distress in patients with cancer	<ul style="list-style-type: none"> • Global Distress Index • MSAS Psychological • MSAS Physiological 	<ul style="list-style-type: none"> • 0–4 • 0 – Not at all • 4 – Very severe/much/often <p>Higher numbers indicate worse outcomes</p>
MVQOLI ⁸	Assess QoL measures in patients with terminal illness	<ul style="list-style-type: none"> • Global • Symptom • Function • Interpersonal • Wellbeing • Transcendent 	<ul style="list-style-type: none"> • Agree Strongly to Neutral/Disagree Strongly <p>Outcome depends on statement to which answer is given</p>
NRS ⁹	Measure severity of symptoms being assessed	<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • 0 – # • 0 – Not at all • # – Worst <p>Higher numbers indicate worse outcomes</p>
POMS ¹⁰	Assess transient, fluctuating feelings and enduring affect states	<ul style="list-style-type: none"> • TMD • Tension-anxiety • Depression • Anger-hostility • Vigor-activity • Fatigue 	<p>TMD</p> <ul style="list-style-type: none"> • 0–6 • 0 – No disturbance • 76 – More disturbance

		<ul style="list-style-type: none"> • Confusion-bewilderment 	Higher numbers indicate worse outcomes
RSCL ¹¹	Assess QoL in patients with cancer	<ul style="list-style-type: none"> • Physical Symptom Distress • Psychological Distress • Activity Level • Overall valuation of life 	<p>Physical Symptom Distress/Psychological Distress</p> <ul style="list-style-type: none"> • 1–4 <ul style="list-style-type: none"> • 1 – Not at all • 4 – Very much <p>Higher numbers indicate higher level of burden or impairment</p> <p>Activity Level</p> <ul style="list-style-type: none"> • 1–4 <ul style="list-style-type: none"> • 1 – Not at all • 4 – Very much <p>Overall valuation of life</p> <ul style="list-style-type: none"> • 1–7 <ul style="list-style-type: none"> • 1 – Excellent • 7 – Very poor <p>Higher numbers indicate worse outcomes</p>
STAI ¹²	Measure presence and severity of current symptoms of anxiety	<ul style="list-style-type: none"> • State Anxiety Inventory Scale • Trait Anxiety Inventory Scale 	<p>State Anxiety Inventory Scale</p> <ul style="list-style-type: none"> • 1–4 <ul style="list-style-type: none"> • 1 – Not at all • 4 – Very much so <p>Trait Anxiety Inventory Scale</p> <ul style="list-style-type: none"> • 1–4 <ul style="list-style-type: none"> • 1 – Almost never • 4 – Almost always <p>Higher numbers indicate worse outcomes</p>
VAS ¹³	Measure severity of symptom(s) being assessed	<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • 0–100mm <ul style="list-style-type: none"> • 0 – Least possible • 100 – Worst possible <p>Higher number indicates worse outcomes</p> <p>(Length of scale may vary)</p>
VSH ¹⁴	Measure previous night's sleep characteristics	<ul style="list-style-type: none"> • Sleep Disturbance • Effectiveness • Supplementation 	<p>Sleep Disturbance/Effectiveness</p> <ul style="list-style-type: none"> • 0–100mm <ul style="list-style-type: none"> • 0 – Better sleep • 100 – Worse sleep

			<p>Higher numbers indicate worse outcomes</p> <p>Supplementation</p> <ul style="list-style-type: none"> • 0–100mm <ul style="list-style-type: none"> • 0 – Worse sleep • 100 – Better sleep <p>Lower numbers indicate worse outcomes</p>
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Table 2. Description of Validated Assessment Tools used in Studies. Table that describes various assessment tools that have been validated in literature. A few studies used tools specific to their institution which could not be found in literature or full access was unavailable. Variations of the listed tools may have been adopted in studies.

CQLS=Current Quality of Life Scale. ESAS=Edmonton Symptom Assessment Scale. GWBS=Global Well Being Scale. HADS=Hospital Anxiety and Depression Scale. MYMOP/MYMOP2=Measure Your Medical Outcomes Profile (Version 2). MPAC=Memorial Pain Assessment Card. MSAS=Memorial Symptom Assessment Scale. MVQOLI=Missoula-VITAS Quality of Life Index. NRS=Numerical Rating Scale. POMS=Profile of Mood States. QoL=Quality of Life. RSCL=Rotterdam Symptom Checklist. SCQLS=Satisfaction with Current Quality of Life Scale. STAI=State-Trait Anxiety Inventory Scale. TMD= Total Mood Disturbance. VAS=Visual Analogue Scale. VSH=Verran and Snyder-Halpern.

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Figure 1
Flow Diagram of Steps in Systematic Review

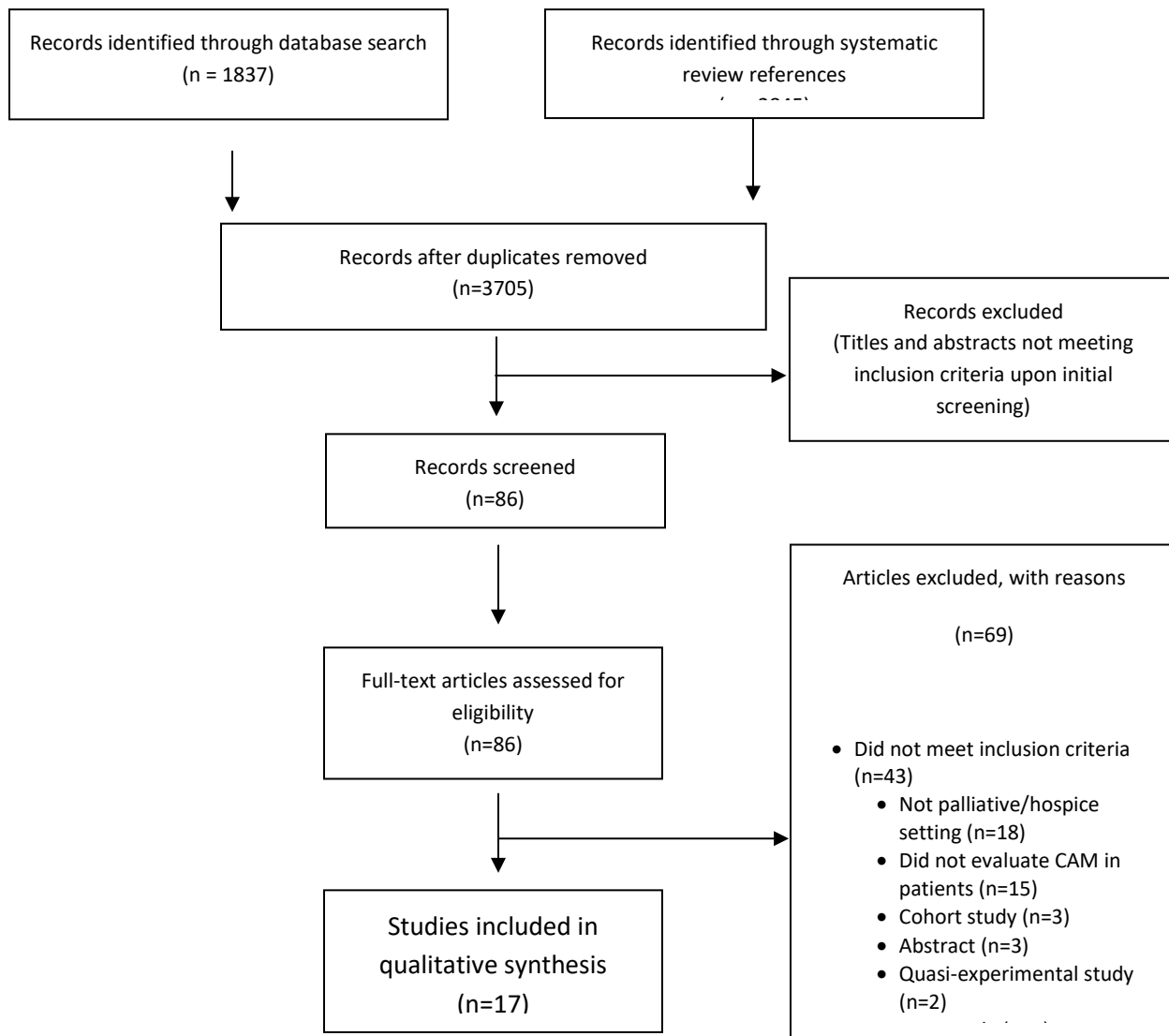


Figure 1. Flow Diagram of Steps in Systematic Review. Outlines steps taken and number of studies excluded and included in each step.

Supplemental Figure 1
Complementary and/or Alternative Medicine Definitions
Embase Emtree

Alternative Medicine
 Aromatherapy
 Horticultural therapy
 Iridology
 Mesotherapy
 Moxibustion
 Orthomolecular medicine
 Reiki
 Shamanism
 Spiritual healing
 Therapy with helminths

PsycINFO Thesaurus

Alternative Medicine
 Biofeedback Training
 Dietary Supplements
 Holistic Health
 Hypnotherapy
 Massage
 Medical Treatment (General)
 Medicinal Herbs and Plants
 Meditation
 Mind Body Therapy
 Osteopathic Medicine
 Phototherapy
 Physical Treatment Methods
 Preventive Medicine
 Shock Therapy
 Transcultural Psychiatry

CINAHL Headings

Alternative Therapies
 Alternative Medical Systems (+3)
 Acupuncture (+4)
 Meridians
 Anthroposophy
 Chiropractic (+1)
 Homeopathy
 Medicine, Herbal (+1)
 Medicine, Oriental (+7)
 Medicine, Ayurvedic
 Medicine, Oriental
 Acupressure (+2)
 Medicine, Chinese (+3)
 Acupuncture (+4)
 Naturopathy
 Apitherapy
 Aromatherapy
 Auriculotherapy (+1)
 Bioelectromagnetic Application (+9)
 Bioenergy Therapies
 Reiki
 Therapeutic Touch
 Bowen Technique
 Butekyo Method
 Detoxification, Alternative Therapy (+2)
 Life Style Changes
 Manual Therapy (+4)
 Chiropractic (+5)
 Massage (+5)
 Reflexology
 Mind Body Techniques
 Guided Imagery
 Hypnosis (+1)
 Meditation
 Music Therapy
 Relaxation Techniques (+2)
 Spiritual Healing (+1)
 Tai Chi
 Yoga (+1)
 Natural and Biologically Based Therapies (+2)
 Medicine, Herbal
 Pharmacological and Biological Treatments
 Rejuvenation
 Wilderness Experience

MEDLINE MeSH

Complementary Therapies
 Acupuncture Therapy
 Acupuncture Analgesia
 Acupuncture, Ear
 Electroacupuncture
 Meridians +
 Moxibustion
 Anthroposophy
 Auriculotherapy (+1)
 Diffuse Noxious Inhibitory Control
 Holistic Health (+1)
 Homeopathy
 Horticultural Therapy
 Medicine, Traditional (+9)
 Mesotherapy
 Mind-Body Therapies
 Aromatherapy
 Biofeedback, Psychology +
 Breathing Exercises +
 Hypnosis +
 Imagery (Psychotherapy)
 Laughter Therapy
 Meditation
 Mental Healing
 Psychodrama +
 Psychophysiology
 Relaxation Therapy
 Tai Ji
 Therapeutic Touch
 Yoga
 Musculoskeletal Manipulations (+4)
 Therapy, Soft Tissue +
 Naturopathy
 Organotherapy (+1)
 Phytotherapy (+2)
 Reflexotherapy
 Sensory Art Therapies
 Acoustic Stimulation
 Aromatherapy
 Art Therapy
 Color Therapy
 Dance Therapy
 Music Therapy
 Play Therapy
 Speleotherapy
 Spiritual Therapies (+10)

Supplemental Figure 1. Complementary and/or Alternative Medicine Definitions. This figure provides examples of therapies according to each database's definition of CAM. This table is not all-inclusive. Includes MEDLINE's Medical Subject Heading (MeSH) Definition of Complementary therapies, Embase's Emtree Definition of Alternative therapies, PsycINFO's Thesaurus Definition of Alternative therapies and Cumulative Index of Nursing and Allied Health Literature (CINAHL)'s Headings Definition of Complementary therapies.